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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,180	02/26/2004	Catherine C. Turkel	17679 (BOT)	9912

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,180	TURKEL ET AL.	
	Examiner	Art Unit	
	VANESSA L. FORD	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-3,6-16,18-20 and 29* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-3, 6-16, 18-20 and 29* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *29 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This action is responsive to Applicant's amendments and response filed September 28, 2011. Claims 1, 9 and 16 have been amended. Claims 4-5, 17 and 21-28 have been canceled.

Claims 1-3, 6-16, 18-20 and 29 are under examination.

Rejections Maintained

2. The rejection of claims 1-3, 6-16, 18-20 and 29 under provisional double patenting is maintained for the reasons set forth on pages 3-4, paragraph 3 of the previous Office Action.

The rejection is reiterated below:

Provisional Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The claims are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19, 27 and 34 of copending Application No. 12/256, 665 filed January 18, 2005 in view of Mathew et al *(Headache 2002, 42;454, Abstract S107).*

This is a provisional obviousness-type double patenting rejection.
This application is drawn to a method of treating an acute pain medication overuse disorder caused by overuse of acute pain medication by administering botulinum toxin to the patients. Co-pending application 12/256,655 is drawn to a method for treating a headache in a triptan medication overuse patient by administering botulinum toxin to the patients.

Co-pending application 10/780,180 does not specifically recite that the medication overusers are triptan medication overusers. However, Matthew et al teach that acute medications that are overused include triptans (the Abstract, 2nd column). Thus, Matthew et al teach triptan medication overusers. Matthew et al teach that botulinum toxin was effective in treating patients with medication overuse by reducing the number of chronic migraine and thereby reducing the acute medication use (see the Abstract).

It would be *prima facie* obvious at the time the invention was made to include triptan medications as a part of the genus of medications that can be overused by medication overusers because Matthew et al teach that triptan medications are among the medications overused by patients that experience chromic migraines (see the Abstract). It would be expected barring evidence to the contrary, that botulinum toxin can be used to effectively treat chronic headaches in triptan medication overuse patients.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's Arguments

Applicant's elect to postpone responding until the rejection is no longer a "provisional rejection".

Examiner's Response to Applicant's Arguments

Applicant's arguments filed September 28, 2011 have been fully considered but they are not persuasive. Applicant did not respond to this rejection and therefore, the rejection is maintained for the reasons of record.

3. The rejection of claims 1-3, 6-16, 18-20 and 29 under 35 U.S.C. 103(a) is maintained for the reasons set forth on pages 5-8, paragraph 4 of the previous Office Action.

The rejection is reiterated below:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The claims are rejected under 35 U.S.C. 103(a) as unpatentable over Bigal et al *(Cephalagia, 2002, 22, p. 432-438)* in view of *Cephalalgia, An International Journal of Headache*, (Volume 24, Supplement 1, 2004) and further in view of Loder et al *(The Clinical Journal of Pain, 18:S169-S176, 2002).*

Independent claim 1 is directed to a method of treating an acute pain medication overuse disorder caused by overuse of acute pain medication, the method comprising the step of local administration of between about 1 unit and about 1500 units of a pure botulinum toxin type A or B, wherein the pure botulinum toxin has a molecular weight of about 150 kDa, to a patient with acute pain medication thereby treating the acute pain medication overuse disorder caused by overuse of acute pain medication, wherein the patient takes the medication prior to experiencing pain and experiences pain after the intake of acute pain medication thereby treating the acute pain medication overuse disorder caused by the overuse of acute pain medication.

Dependent claim 29 is drawn to the method of claim 16, wherein the patient experiences a headache frequency greater than 15 days per month after the intake of analgesics or ergots more than 15 times per month for at least 3 months.

Loder et al teach that administration of botulinum toxin decreases that pain and provides relief for patients suffering from chronic daily headaches (see the Abstract and S172-S173).

Loder et al do not specifically teach the claim limitation “wherein the patient experiences a headache frequency greater than 15 days per month after the intake of analgesics or ergots more than 15 times per month for at least 3 months”.

Bigal et al teach patients that are medication overusers that suffer from chronic daily headaches (page 434, 1st column, Table 1). Bigal et al teach chronic daily headache (CDH) is a headache lasting more than 4 hours per day and on 15 or more days per month (page 432, 1st column).

Cephalalgia, An International Journal of Headache, Volume 24, Supplement 1, 2004 teach that the most common migraine-like headache occurs on ≥ 15 days per

month and occur as a mixture of migraine-like and tension-like headaches (page 94). *Cephalalgia, 2004* teach that these patients overuse migraine drugs and /or analgesics (page 94). *Cephalalgia, 2004* teach that diagnostic criterion is used on ≥ 10 days per month, this translates into 2-3 treatment days a week (page 94).

It would have been prima facie obvious at the time the invention was made to modify the method of treating chronic daily headaches as taught by Loder et al to include patients that have chronic daily headache and are medication overusers because *Cephalalgia, 2004* teach that medication overuse patients are patients that use migraine or analgesics on ≥ 10 days per month, this translates into 2-3 treatment days a week and Loder et al teach that administration of botulinum toxin decreases that pain and provides relief for patients suffering from chronic daily headaches. It would be expected, absent evidence to the contrary that botulinum toxin would be effective in treating patients with chronic daily headaches (patients that have a headache for at least 4 hours per day) including patients that suffer from medication overuse.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method, and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art that patients that suffer from medication overuse have chronic daily headaches and chronic daily headache patients are patients that have a headache for at least four hours per day for ≥15 days/per month. See Bigal et al. It well known in the art that medication overuse patients are patients that have the diagnostic criterion of headaches on ≥ 10 days per month which translates into 2-3 treatment days a week. See of *Cephalalgia, An International Journal of Headache*, (Volume 24, Supplement 1, 2004). It is also well known in the art to treat patients who suffer from chronic daily headaches with botulinum toxin. See Loder et al.

Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results. The combination of prior art references as combined provided a *prima facie* case of obviousness absent convincing evidence to the contrary.

Applicant's Arguments

Applicant urges that to establish a prima facie case of obviousness under 35 U.S.C. 103, the Office must show a suggestion, teaching or motivation to combine prior art references with a reasonable expectation of success.

Applicant urges that the Bigal reference reviews the International Headache Society diagnostic criteria for chronic daily headaches and proposes revisions to those criteria Applicant urges that Bigal does not teach or suggest the administration of botulinum toxin to treat headaches in triptan medication overuse patients.

Applicant urges the cited Cephalagia 2004 reference presents prospective diagnostic criteria for medication-overuse headaches. Applicant urges that the reference does not teach or suggest specific methods of treating such headaches and certainly does not teach the administration of botulinum to treat triptan medication overuse headaches.

Applicant urges that Loder teaches the use of botulinum toxin to treat migraine headaches, chronic daily headaches (defined as more than 15 days per month), tension-type headaches and post-whiplash headaches. Applicant urges that Loder does not teach or suggest the use of botulinum toxin to treat triptan medication overuse headaches wherein both the headache exacerbation caused by the triptan overuse and the actual use of triptan medication is treated by botulinum toxin. Applicant urges that in addition these references fail to teach the specific range of administering between 105 and 260 units of botulinum toxin. Applicant urges that Loder reference teach away from the claimed invention. Applicant urges that Loder administers 25 units and labels the 75 unit treatments as ineffective.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed September 28, 2011 have been fully considered but they are not persuasive.

In response to applicant's argument that no case of prima facie obviousness has been made, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, Bigal et al teach patients that are medication overusers that suffer from chronic daily headaches and Bigal et al teach chronic daily headache (CDH) is a headache lasting more than 4 hours per day and on 15 or more days per month. Bigal et al do not specifically teach the claim limitation "wherein the patient ingests triptan medication of at least ten days a month and at least twice a week". *Cephalalgia, An International Journal of Headache*, Volume 24, Supplement 1, 2004 teach that the most common migraine-like headache occurs on ≥ 15 days per month and occur as a mixture of migraine-like and tension-like headaches and *Cephalalgia, 2004* teach that these patients overuse migraine drugs and /or analgesics. *Cephalalgia, 2004* teach that diagnostic criterion is used on ≥ 10 days per month, this translates into 2-3 treatment days a week. However, Loder et al

teach that administration of botulinum toxin decreases that pain and provides relief for patients suffering from chronic daily headaches.

One of ordinary skill in the art would have been motivated at the time the invention was made to modify the method of treating chronic daily headaches as taught by Loder et al to include patients that have chronic daily headache and are medication overusers *Cephalalgia, 2004* teach that medication overuse patients are patients that use migraine or analgesics on ≥ 10 days per month, this translates into 2-3 treatment days a week and Loder et al teach that administration of botulinum toxin decreases that pain and provides relief for patients suffering from chronic daily headaches. The combination of prior art references have established that populations of patients that have chronic headaches are medication overuser patients and these overuser patients can be treated with administration of botulinum toxin. The combination of references have also established that administration of botulinum toxin decreases that pain and provides relief for patients suffering from chronic daily headaches.

To address Applicant's comments regarding the Loder not teaching the recited doses of about 105 units and about 260 units of pure botulinum toxin A or B, Loder teaches that about 25-100 units are divided among the injection sites. See page S172, Figure 1. Thus, Loder does teach the doses that fall within applicant's recited administration range used in the claimed invention.

The Examiner disagrees with Applicant's assertion that Loder teaches away from the claimed invention because Loder teaches that botulinum toxin is safe and does not

produce systemic effects associated with other types of headache treatments. See the Abstract.

KSR International Co. v. Teleflex Inc., 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method, and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. It is well known in the art that patients that suffer from medication overuse have chronic daily headaches and chronic daily headache patients are patients that have a headache for at least four hours per day for ≥15 days/per month. See Bigal et al. It is well known in the art that medication overuse patients are patients that have the diagnostic criterion of headaches on ≥ 10 days per month which translates into 2-3 treatment days a week. See of *Cephalalgia, An International Journal of Headache*, (Volume 24, Supplement 1, 2004). It is also well known in the art to treat patients who suffer from chronic daily headaches with botulinum toxin. See Loder et al.

It should be remembered that *KSR Intl'* discloses that if a technique has been used to improve one method, and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. The presently claims invention is not beyond the skill of the ordinary artisan based on the upon the knowledge in the art regarding, populations of headache patients including medication overuse patients and in particularly triptan medication overusers. It is not beyond the level of the artisan of ordinary skill to administer botulinum toxin to patients that are triptan medication

overusers to treat these patients from that disorder based on what was known in the art at the time the invention was made.

The Examiner has established that there is a populations of patients that have acute medication overuse disorder which suffer from chronic daily headaches and that administration of botulinum toxin is used to treat these headaches as well as the acute medication overuse disorder in these patients.

It should be noted that in the prosecution history of application 11/039,506 which is a continuation in part of this application, the Board of Patent Appeals and Interferences affirmed the Examiner on the rejection of Bigal, Cephalagia and Loder.

Independent claims 1 is directed to a method for treating a headache in a triptan medication overuse patient, the method comprising the step of local administration of about 1 to 1500 units of botulinum toxin to a patient who is a triptan medication overuse patient, wherein the patient ingests triptan medication of at least ten days a month and at least twice a week, thereby both countering a headache exacerbation caused by triptan medication overuse and reducing the use of triptan medication by the patient to treat the headache.

Independent claim 9 is directed to a method for treating a headache in a triptan medication overuse patient, the method comprising the step of local administration of between about 1 to 1500 units of botulinum toxin A to a patient who is a triptan medication overuse patient, wherein the patient experiences headaches having a duration of at least four hours and ingests triptan medication of at least ten days a month and at least twice a week, thereby both countering a headache exacerbation caused by triptan medication overuse and reducing the use of triptan medication by the patient to treat the headache.

The Board stated:

"In sum, as Appellant's arguments do not persuade use that the Examiner erred in concluding that claim 1 would be obvious to an ordinary artisan, we affirm the Examiner's obviousness rejection of claim 1 as well as claims 2, 3 and 5-9 which were argued in the same groupings as claim 1". See page 12 of the decision (which is enclosed with this action).

"Given these teachings, we agree with the Examiner that an ordinary artisan having administered to a triptan to treat a chronic daily headache lasting for at least four hours, or suffering from a chronic daily headache lasting for over four hours that resulted from triptan overuse, would have been prompted by Loder to also administer botulinum toxin to treat the headache. As we agree with Examiner that an ordinary artisan would have considered it obvious to administer botulinum toxin to a triptan-taking patient to treat a headache lasting at least four hours, we further agree that claim 10 would have been prima facie obvious to an ordinary ordinary artisan". See pages 12-13 of the board decision.

The combination of prior art reference teach the claims invention, absent convincing evidence to the contrary.

In view of all of the above, this rejection is maintained.

New Ground of Rejection Necessitated by Applicant's Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3, 6-16, 18-20 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.* The amendment filed August 11, 2009 introduces new matter into the claims.

Claim 1 recites "…the method comprising a step of local administration by intramuscular or subcutaneous administration to location on or within a head of a patient of *between about 105 and about 260 units of a pure botulinum type A or type B toxin*...". These claim limitations are not supported by the instant specification.

35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention.

Applicant referred the Examiner to pages 34-35 of the originally filed specification.

The instant specification discloses that “the BOTOX was administered to seven different muscles”. The instant specification discloses that "from 105 to 260 units of BOTOX was administered to each patient at each of three treatment sessions”. See page 42, Example 1. The instant specification disclose "to guide the practitioner, typically, no less than about 1 unit and no more than about 25 units of a botulinum toxin A (such as BOTOX®) is administered per injection site (i.e. to each muscle portion injected), per patient treatment session. For a botulinum toxin type A such as DYSPORT®, no less than about 2 units and no more about 125 units of the botulinum toxin type A are administered per rejection site, per patient treatment session. For a botulinum toxin type B such as MYOBLOC®, no less than about 40 units and no more about 1500 units of the botulinum toxin type B are administered per injection site, per patient treatment session”. See page 35.

The specification fails to disclose the newly added claim limitations. Currently amended claims 1 and 9 do not teach that *multiple sites* were injected to account for the total of about 105 to 260 units administered of botulinum toxin given per treatment session as indicated by the specification. Applicant is required to cancel the new matter in the reply to this Office Action.

Status of Claims

5. No claims allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to VANESSA L. FORD whose telephone number is (571)272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/VANESSA L FORD/
Primary Examiner, Art Unit 1645
December 13, 2011